DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER
585 Commercial St.
Boston, MA. 02109

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	DATE OF INSPECTION	C. F. NUMBER
TO: Robert T. Schooley, M.D.	10/14-17,20-24,27-30 11/10-12/86	
TITLE OF INDIVIDUAL: Clinical Investigator	TYPE ESTABLISHMENT INSPECTED: same	
FIRM NAME: Mass. General Hospital	NAME OF FIRM, BRANCH OR UNIT INSPECTED: Infectious Disease Unit	
STREET ADDRESS: Fruit St.	STREET ADDRESS OF PREMISES INSPECTED: same	
CITY AND STATE: Boston, MA. 02114	CITY AND STATE: same	

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

Records were reviewed for 14 subjects.

1.) Deaths and adverse reactions were not reported to the IRB (Human Studies Committee). There have been two deaths, each after the subject was off the study medication. Adverse reactions have included seizure (thought to be unrelated), dizziness, severe coughing, etc.

2.) There is no documentation to verify that calls were made promptly to notify sponsor of deaths or severe adverse reactions.

3.) Deviations from the Protocol were alledgedly approved per telcons.
These calls were not documented, or noted in the case report forms (CRF's). These deviations from the Protocol were not reported to the IRB:

A. Concurrent Medication
1001: Cefadroxil, Erythromycin (within 2 wks prior to the study);
1003: Acyclovir, Wacomil, Ranitidine (Zantac);
1005: Hydrocortisone Cream (topical),Benadryl, Dilantin;
1006: Stelazine, Xanax, Halcion, Colace;
1008: Compazine, Tylenol, Lomotil;
1009: Tylenol;
1011: Benadryl, Excedrin;
1012: Keflex;
1051: Erythromycin;
1055: Streptomycin, INH (Isoniazid), Ethambutol, Pyridoxine;
1057: Lithium;

B.) There is no documentaion of "Special permission" recieved to admit no. 1011 since the timing o[redacted] was outside the protocol requirements.
No. 1055 was diagnosed as having [redacted] by [redacted] but MGH decided it was not. However clinical investigator did not so document on

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	Patricia A. Spitzig	Patricia A. Spitzig Investigator

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the CRF's and subject was classified as [redacted]atient.

C.) Tests for the following eleven subjects were not done as frequently as called for in the protocol: 1004, 1005, 1006, 1008, 1009, 1011, 1012, 1051, 1053, 1055, 1057.

Adverse reactions:

4.) Adverse reaction of high SGOT is not mentioned on CRF for 1003 (CRF p.73 says "none").

1004 Severe coughing not addressed if adverse reaction or not in CRF, (wk.14).

1004 and [redacted] were treated in the Emergency Room during the study due to need for blood.

1005's ataxia and "wobbly-transient" were not reported as adverse reactions, nor explained.

1008 was hospitalized during the study, which was not stated in CRF's and was said to have no adverse reactions. Wks. 1, 2, 3, 4, 8, 10, 12 had moderate headaches, diarrhea, lethargy, abdominal cramps, dizziness, but no adverse reactions.

1012 had rash wk 8, but no adverse reaction; wk 10 had moderate loss of appetite, no adverse reaction.

1051 had SGPT value of 58 during wk 3, and in wk 4, SGPT value of 57, but no adverse reactions.

1053 wk 2 listed nausea and marked fatigue, but no adverse reactions; wk 3 WBC's were 1.6 and granulocytes were 944, but no adverse reactions. During wks 10 and 12, Pt. diary says blood counts were too low to take the drug, but adverse reaction CRF says patient took drug during part of that time. 14 WBC 1.6; no adverse reaction.

1059 went to the emergency room during the study and had NMR and CT tests, but this is not stated in the CRF's, nor are there any adverse reactions.

CRF's

5.) Changes that are not dated initialed or explained have been made on photocopied CRF's (raw records) after the original was

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taken by the monitor. CRF's rarely state who did the work, or who made the entries on the pages. The research nurse who made many entries was replaced by another nurse for two weeks, but it is not possible to determine that from the records.

Opportunistic infection forms frequently state re: onset date, "(per sponsor's request), (seen earlier)".

6.) There is no comment by the clinical investigator re several significant observations (including sujbect left the study) and abnormal values, eg.:

1003: IgG value out of range (high - 2589, Range 540-1480), wk 12;

Note of "neck mass" not explained, initialed, dated at wk 20 (noted on study med record). When it was explained on record 2 wks later, there were no initials and the subject was removed from the study.

1055: "fevers to 105 - admitted to hospital. Drug held", CRF not say why ended study.

1056: a placebo subject, received 1057's medication [redacted] for two weeks, this is not explained on his 1056's CRF. 1057's record does not reflect this. There should be an extra bottle of 100 for 1056, but it is not accounted for.

1057: had HGB value below entrance criteria; repeat HGB value was used instead.

1059: not say why ended study.

7.) Several raw data records (other than CRF's) could not be located to support data in CRF's. The research nurse said if they are missing they were thrown out, eg.

1011: hematology at preentry.

8.) Recordsof HTLV III test results from CI's lab do not state where or by whom the tests were done or the record was generated.

ACCOUNTABILITY

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9.) Shipment records do not state clearly what was sent and they were not verified with the shipment. No one recalls one shipment of placebos in envelopes (ordinarily the medicine was in amber bottles). Records are not sufficient to allow-comparison test article useage versus the amount shipped, and as compared to the amount returned to the sponsor.

To the best of our knowledge, records of shipment indiated 87 more containers (of 50 or 100 capsules each) were shipped than were received by the pharmacy.

10.) Pharmacy inventory of study medication not kept by #units in bottles; running inventory record was destroyed. A shipment of bottles with a handwritten "50" on the label was not documented.

11.) Medication returned by subjects were not counted at the time; estimates of amount returned were changed on many CRF's for 10 subjects.
Returned medication was not always stored in a locked/secured area/cabinet.
Statement of returned study medication is signed by monitor instead of the clinical investigator.

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